

**REMARKS**

Claims 15, 17-18, 20-23, 32-33 and 37, 39-45 are now in the case.

**Amendment to the claims**

Reconsideration of this Application and entry of the foregoing amendments are requested. Claims 17, 20, 32, 39, 41 and 42 have been amended, claims 43 to 45 have been added in view of the Office Action and to better define what the Applicants consider their invention, as fully supported by an enabling disclosure. Support for modifications to the claims may be found in previously presented claims.

**Rejections under 35 U.S.C. §112, second paragraph**

The Examiner rejects claims 17-18, 20-23, 39 and 41-42 under 35 U.S.C. § 112, second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner is of opinion that claims reciting the term "directly" are indefinite/unclear with regard to the candidate compound altering of resistance. Claims 20 and 39 were amended accordingly to remove the term "directly".

Claim 20 was amended to recite the full name of MDR pursuant to the Examiner's request.

Claims 17, 18, 41 and 42 are rejected as being confusing because they are markush claims listing both polynucleotide and protein members and because of double inclusions of certain members. These claims have been reformulated to remove apparent double inclusions and to list only polynucleotide members. New claims 43 to 45 a markush claims listing only protein members.

Claim 32 and other claims with the language "increase in the expression of an annexin protein, whereby said increased expression is capable of conferring MDR" are rejected because they are allegedly indefinite. In order to accelerate prosecution, claim 32 was amended to recite the wording "confers MDR" as suggested by the Examiner (see paragraph 7 of the Office Action).

### Rejections under 35 U.S.C. §103

Applicants gratefully note that the rejection of record under §102/103 rejection was withdrawn in favor of a § 103 rejection. Applicants also note that claims 18, 21-23 and 41-45 are free of the prior art.

The Examiner rejects claims 15-17, 19-20, 32, 33 and 37-40 under 35 U.S.C. § 103. The Examiner remains of the opinion that these claims are obvious over Wang. Applicants first note that claim 19 was cancelled in the response filed on July 25, 2003. The Applicants respectfully disagree as follows:

The Examiner alleges that “[a]lthough Wang does not teach a direct correlation [...], it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole because Wang teaches an *indirect correlation* and that P-40 is important in the expression of drug resistance phenotype, thus provides a suggestion for a direct correlation.” [Our emphasis]. It is respectfully submitted that Wand does not teach any correlation at all be it direct or indirect. All that Wang shows is that an overexpression of P-40 was observed in cells displaying multidrug resistance (MDR). Wang does not show that these two characteristics of the tested cells are linked in any way or that one characteristic (i.e. overexpression of P-40) is the cause of the other (i.e. MDR). It is reiterated that from the results presented in Wang, it was not possible to determine whether the overexpression of P-40 was due to gene amplification (as is often the case in cells treated with anti-cancer drugs: they produce multiple copies of genes as a cell survival mechanism) or to any other event unrelated to MDR or to P-40 mRNA. It is further that Wang’s observations do not demonstrate that Annexin’s overexpression confers MDR. Results showing that a cell that is sensitive to a cytotoxic drug that is transfected with a recombinant Annexin DNA (See Figures 6 to 9 and their legends at page 18, line 19 to 19, line 29; page 23, lines 8 to 28; and most particularly, page 29 line 6 to page 30, line 2; and page 33, lines 1 to 4) becomes resistant to this drug after transfection were necessary to show that annexin confers MDR. Such results were necessary to show that Annexin is a cause of multidrug resistance.

It is reiterated that results presented in Wang simply provide an incentive to pursue experiments. Although it may be said that from Wang’s results it was *obvious to try* to show that P-40 caused MDR -- this is not however the test for 5579308\_1.DOC

determining obviousness. The applicable test for determining obviousness is more stringent: it requires that there be a good likelihood of success for the claimed subject matter in light of what was known in the art. It is submitted that the field of the present invention is a highly unpredictable field where solid experimental results are necessary in order to come to any credible conclusion. It is thus further reiterated that results presented in Wang would not have enabled a person of ordinary skill to come to the conclusion that P-40 caused MDR without undue experimentation. Wang's authors themselves did not come to this conclusion. They admitted that additional work was necessary in order to verify their hypothesis. Indeed, as indicated earlier, it required 5 years for the Applicants to obtain the results presented in the present application that were necessary for them to conclude that Annexin indeed caused MDR and that inhibiting Annexin would reduce MDR.

### **Conclusions**

The rejections of claims 15-23, 32, 33 and 37-42 are believed to have been overcome by the present remarks, and by the amendments to the claims. From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such an action is earnestly solicited.

In the event that there are any questions concerning the Amendment, or application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedited.

Authorization is hereby given to charge Deposit Account no. 17-0055 for any deficiencies or overages in connection with this Response.

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By:

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